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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/967,237	ZAVADA ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-27,30-51 and 53-55* is/are pending in the application.

4a) Of the above claim(s) *24-27,32-35,39-41,44,45 and 49-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22, 30, 36-38, 42-43, 46-48 and 53-55* is/are rejected.

7)☒ Claim(s) *23 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S-003

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 15 June 2005 has been entered.

2. Claims 22-27, 30-51 and 53-55 are pending.

Claims 22, 30 and 42 have been amended.

Claims 53-55 have been added.

Claims 24-27, 32-35, 39-41, 44-45 and 49-51 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

3. Claims 22-23, 30-31, 36-38, 42-43, 46-48 and 53-55 are under examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This Office Action contains New Grounds of Rejections.

Rejections Withdrawn

6. The rejection of claims 22-23, 30-31, 36-38, 42-43 and 46-48 under 35 U.S.C 103(a) as being unpatentable over Pastorekova et al as evidenced by Pastorek et al in

view of Raychaudhuri et al is withdrawn in view of applicant's arguments and the declarations in the response filed 4/13/05.

7. The rejection of claims 22, 30, 36-38, 42-43 and 46-48 under 35 U.S.C 103(a) as being unpatentable over Oosterwijk et al [a] as evidenced by Uemura et al and as evidenced by Pastorek et al in view of Raychaudhuri et al is withdrawn in view of applicant's arguments, i.e., pertaining to the lack of enablement and availability of the hybridoma producing the G250 monoclonal antibody, which was not deposited until after the earliest priority date of the instant application, as evidenced by page 2 of WO 02/062972 filed 4/13/05 (Appendix 3).

8. The rejection of claims 22, 30, 36-38, 42-43 and 46-48 under 35 U.S.C 103(a) as being unpatentable over Oosterwijk et al [b] as evidenced by Uemura et al and as evidenced by Pastorek et al in view of Raychaudhuri et al is withdrawn in view of applicant's arguments, i.e., pertaining to the lack of enablement and availability of the hybridoma producing the G250 monoclonal antibody, which was not deposited until after the earliest priority date of the instant application, as evidenced by page 2 of WO 02/062972 filed 4/13/05 (Appendix 3).

Response to Arguments

9. The rejection of claims 22, 30, 36-38, 42-43 and 46-48 and applied to newly added claims 53-55 under 35 U.S.C. 112, first paragraph because the specification does not enable any person skilled in the relevant art to which it pertains, or with which

it is most nearly connected, to make or use the invention commensurate in scope with the claims is maintained and made again.

The response filed 6/15/2005 has been carefully considered, but is deemed not to be persuasive. The response argues that base claims 22, 30 and 42 have been amended to recite that the claimed anti-idiotype antibody "comprises an internal image corresponding to said epitope" of an MN protein or MN polypeptide meaning that the anti-idiotypic antibody comprises an immunogenic functional mimic of an MN protein epitope and the phrase "comprises an internal image corresponding to said epitope of said MN protein/polypeptide", also means that the claimed anti-idiotype antibody is immunogenic and that antibodies elicited by the claimed anti-idiotype antibody "cross-react with naturally occurring MN proteins and polypeptides to a sufficient extent to provide protective immunity and/or anti-tumorigenic activity when administered as a vaccine (page 82, lines 19-21 of the specification). Applicant concludes that as amended the claims only refer to anti-idiotype antibodies that mimic the linear conformational epitopes of the native MN protein. In response to these arguments, the claims remain broadly drawn to anti-idiotypic antibodies to a second antibody that binds any MN protein epitope (i.e., any fragment of the MN protein) and MN proteins and polypeptides that would not mimic the epitopes of the native MN protein of SEQ ID NO:2 encoded by SEQ ID NO:1 or encoded by polynucleotides that differ from SEQ ID NO:1 due to the degeneracy of the genetic code. While it is acknowledged that the advisory action mailed 4/27/05 indicated that applicant's response filed 4/13/2005, if entered, would overcome the instant enablement rejection as applied to claims 22 and

46, however claims 22 and 46 as presently amended still encompass a myriad of MN protein epitopes or MN protein fragments and MN proteins and fragments which are not encoded by SEQ ID NO:1 (i.e., polynucleotides that differ from SEQ ID NO:1 due to the degeneracy of the genetic code), and are not enabled for reasons of record and reiterated herein. Additionally, claims 30, 36-38, 42-43, 46-48 and 53-55 broadly encompass essentially any fragment of the MN protein (i.e., polynucleotide containing at least 29, 50, 100, 150, 25 or 27 nucleotides) as well as MN proteins and fragments that are not encoded by SEQ ID NO:1 (i.e., differ from SEQ ID NO:1 due to the degeneracy of the genetic code) since the claims do not require the polynucleotides that differ from SEQ ID NO:1 due to the degeneracy of the genetic code to actually encode the MN protein of SEQ ID NO:1. As set forth in the previous Office Actions, Applicant as well as the art recognizes that the antigen mimicry properties of an anti-idiotypic antibody is dependent upon its three-dimensional conformation that resembles the structure of the natural antigen (MN protein in this case). Further the specification states that Ab2 mimicking the normal antigen (so-called internal image Ab2) may be used as surrogate antigen for vaccination to trigger the host's immune system specifically against the nominal antigen (see page 75). Again, Applicant has not provided or pointed to any objective evidence that just any MN fragment of SEQ ID NO:1 or MN protein epitopes/MN fragments not encoded by SEQ ID NO:1 as defined by the claims would mimic the structure of the natural MN protein of SEQ ID NO:2 expressed on the surface of renal cell carcinomas wherein antibodies that bind these MN fragments contain idiotypes and anti-idiotypic antibodies produced against these idiotypes mimic the three-

dimensional structure of the natural MN protein of SEQ ID NO:2. One of skill in the art would not expect nor predict the appropriate functioning of antibodies elicited by the claimed anti-idiotype antibodies defined by the claims to cross-react with the naturally occurring MN protein of SEQ ID NO:2 expressed in renal cell carcinomas to a sufficient extent to provide protective immunity and/or anti-tumorigenic activity when administered as a therapeutic composition.

Additionally, as amended the claims recite MN protein epitopes and MN fragments (i.e., polynucleotide containing at least 29, 50, 100, 150, 25 or 27 nucleotides) that are encoded by "polynucleotides that differ from SEQ ID NO:1 due to the degeneracy of the genetic code". The specification does not disclose any polynuceotide that encodes a polypeptide or protein having an epitope that is similar to an epitope of SEQ ID NO:2 (the MN protein), what this epitope actually is or any polynucleotide that encodes an MN protein, that is not the MN protein of SEQ ID NO:2 as broadly encompassed by the claims. The specification teaches methods for identifying polynucleotides that are similar to SEQ ID NO:1, which in essence, simply directs those of skill in the art to go figure out for themselves how to use the myriad of polynucleotides and the encoded polypeptides as a starting point for the production and use of anti-idotypic antibodies as a therapeutic composition in the treatment of renal cell carcinomas, which without more precise guidelines, amount to little more than "a starting point, a direction for further research." *Genentech*, 108 F.3d at 1366. *See also Calgene*, 188 F.3d at 1374 ("the teachings set forth in the specification provide no more than a 'plan' or 'invitation' for those of skill in the art to experiment practicing [the

claimed invention]; they do not provide sufficient guidance or specificity as to how to execute that plan"); *National Recovery Technologies*, 166 F.3d at 1198 (stating that patent-in-suit "recognizes a specific need... and suggests a theoretical answer to that need. It provides a starting point from which one of skill in the art can perform further research in order to practice the claimed invention, but this is not adequate to constitute enablement"). The instant specification does not describe the claimed invention in terms that will "enable any person skilled in the art... to make and use" the invention commensurate in scope with the claims. At most, the specification will enable a person of ordinary skill in the art to attempt to discover how to practice the claimed invention. The specification provides no guidance or direction to assist the skilled artisan in selecting polynucleotides containing at least 29, 50, 100, 150, 25 or 27 nucleotides of SEQ ID NO:1 as an epitope of an antibody wherein anti-idiotypic antibodies to said antibody mimics the structures of the native MN protein expressed in renal cell carcinomas and wherein an immune response elicited by the anti-idiotypic antibody cross-reacts with the native MN protein expressed in renal cell carcinomas. In view of the specification at page 2, which states that the MN protein (i.e., SEQ ID NO:2) is the first tumor-associated carbonic anhydrase described and in view of the absence of objective evidence of other carbonic anhydrases similar to the MN protein that are also tumor-associated and thus, useful as therapeutic compositions (i.e., as an anti-idiotype) and without more specific guidance and direction as to how one of skill in the art would find such sequences as well as identify a correlation of the identified 'similar sequence' to tumors, one of ordinary skill in the art would be forced into undue experimentation.

Applicant is enabled for anti-idiotypic antibodies of the beta type (i.e., $Ab_2\beta$ or internal image) to an idiotype of a second antibody that specifically binds to an epitope of the native MN protein of SEQ ID NO:2 that is encoded by SEQ ID NO:1 or encoded by polynucleotides that differ from SEQ ID NO:1 due to the degeneracy of the genetic code.

New Grounds of Objections/Rejections

10. Claims 47-48 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form. Claims 47 and 48 depend from claims 30 and 42, which recite that the nucleic acid encoding the MN polypeptide contains at least 29 nucleotides and at least 25 nucleotides, respectively. Claims 47 and 48 recite that the nucleic acid "has a nucleotide sequence from SEQ ID NO:1", which could be as few as two nucleotides. Thus, claims 47 and 48 do not include every limitation of the claim on which they depend, i.e., the limitation that the polynucleotides contain at least 29 and 25 nucleotides as recited in base claims 30 and 42 and as such, claims 47-48 do not further limit claims 30 and 42 from which they depend.

11. Claims 22 and 53-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 22 recites the limitation "said MN protein". There is insufficient antecedent basis for this limitation in the claim. The claims recite "an MN protein epitope", which is only part of the MN protein and is not the MN protein. Further, SEQ ID NO:1 encodes the MN protein and not an MN protein epitope as recited.

b. Claims 53-55 are indefinite in the recitation of "biologically active antibody fragment" because it is unclear what biological activity is contemplated by the phrase. Is the biological activity of the antibody fragment mean antigen-binding activity, or the induction of an immune response, or does the antibody fragment have an enzymatic activity as in the case of catalytic antibodies or is some other biological activity contemplated by the phrase? As written, one skilled in the art would not be reasonably apprised of the metes and bounds of the claims.

12. Claims 22, 30, 36-38, 42-43, 46-48 and 53-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied

through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The claims are drawn to internal image anti-idiotypic antibodies that bind to a second antibody ~~antibody~~ wherein the idiotype of the second antibody specifically binds to an MN protein epitope or an epitope of an MN polypeptide, wherein the MN protein is encoded by SEQ ID NO:1 or by polynucleotides that differ from SEQ ID NO:1 due to degeneracy of the genetic code and wherein the MN polypeptide is encoded by a polynucleotide containing at least 29, 50, 100, 150, 25 or 27 nucleotides of SEQ ID NO:1 or by polynucleotides that differ from SEQ ID NO:1 due to degeneracy of the genetic code. The specification only discloses an MN protein having the polynucleotide sequence of SEQ ID NO:1, which encodes the MN protein of SEQ ID NO:2 (see Figure 1 and Brief Description of the Figures at page 23 of the specification). The specification also states that the MN protein is considered to be the first tumor-associated carbonic anhydrase isoenzyme that has been described (see page 2). The specification provides insufficient written description for the broad genus of MN protein epitopes, MN proteins and MN polypeptides that are encoded by polynucleotides that differ from SEQ ID NO:1 due to the degeneracy of the genetic code. The genus of proteins encoded by

polynucleotides that differ from SEQ ID NO:1 due to the degeneracy of the genetic code may have very different structures and functions than the MN protein of SEQ ID NO:2 and the phrase MN protein/polypeptide is insufficient to distinguish members of the genus from those excluded. There is insufficient written description encompassing the MN protein epitopes, MN proteins and MN polypeptides encoded by polynucleotides that differ from SEQ ID NO:1 due to degeneracy of the genetic code because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics that could distinguish members of the genus are not set forth in the specification as-filed, commensurate in scope with the claimed invention. Conception does not occur unless one has a mental picture of the structure of the molecule, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116).

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddles v.Baird, 30 USPQ2d 1481, 1483. In Fiddles v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences.

Therefore, only the MN protein of SEQ ID NO:2, encoded by polynucleotides that differ from SEQ ID NO:1 due to the degeneracy of the genetic code and encoded by SEQ ID NO:1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

13. Claims 22, 30, 36-38, 42-43, 46-48 and 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oosterwijk et al [a] (WO 88/08854, Publication date 11/17/1988, Ids 10/19/2001) as evidenced by Uemura et al (British journal of Cancer, 81(4):741-746, 1999, cited on PTO-892 mailed 3/22/04) and Pastorek et al (Oncogene, 9:2877-2888, 1994, Ids 10/19/2001) and in view of Raychaudhuri et al (US Patent 5,270,202, 3/12/91, cited previously).

The claims are interpreted as being drawn to an anti-idiotypic antibody to an antibody (i.e., second antibody) which specifically binds the MN protein (SEQ ID NO:2) encoded by SEQ ID NO:1. Applicant is reminded that "comprising" and 'containing" are open-ended or inclusive to unrecited elements in the claims (MPEP 2111.03). Thus, for

this rejection the claims which recite wherein the MN polypeptide is encoded by a polynucleotide containing at least 25, 27, 29, 50, 100, 150 nucleotides read on the full-length MN polypeptide/protein (i.e., SEQ ID NO:2). Further, for this rejection the phrase "biologically active antibody fragment" is interpreted to be an antigen-binding antibody fragment.

Oosterwijk et al [a] teach a method for producing monoclonal antibodies and antigen-binding fragments thereof against the G 250 antigen present on renal cell carcinoma carcinomas (RCC) and absent on normal adult fetal kidney tissue (see Example 1 at pages 15-16 and pages 2, 11-12). As evidenced by Uemura et al the G 250 antigen is identical to MN protein of the present claims (also known as carbonic anhydrase IX; CA IX or CA9) (see page 744, left and right column) and as evidenced by Pastorek et al the MN protein sequence is encoded by SEQ ID NO:1. Thus, as evidenced by Uemura et al and Pastorek et al the G 250 antigen is identical to the MN protein of the present claims and is necessarily encoded by the nucleic acid of SEQ ID NO:1. Oosterwijk et al [a] not specifically teach an anti-idiotype antibody to an antibody that specifically binds the MN protein. This deficiency is made up for in the teachings of Raychaudhuri.

Raychaudhuri teaches that immunization with anti-idiotype antibodies of the beta type ($Ab_2\beta$), bearing the internal image of a tumor antigen, induces tumor-specific immunity and can inhibit tumor growth (see columns 14-15 and column 2, lines 14-17) and methods for generating such anti-idiotype antibodies are well known to those of skill in the art (see column 2, liens 63-65). Raychaudhuri teach that fro tumor

immunotherapy anti-idiotypic antibodies as tumor antigen surrogates have a number of advantages, including the ability to manufacture such antibodies in large quantities and increased immunogenicity as compared to natural antigens (see column 3, lines 15-34).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced anti-idiotypic antibodies of the beta type to an antibody that specifically binds the MN protein for active immunotherapy in RCC patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced anti-idiotypic antibodies of the beta type to an antibody that specifically binds the G 250 protein for therapeutic benefit in RCC patients in view of Oosterwijk et al [a] as evidenced by Uemura et al and as evidenced by Pastorek et al in view of Raychaudhuri because Oosterwijk et al [a] a process for producing monoclonal antibodies and antigen-binding fragments thereof against the G 250 antigen present on RCCs and absent on normal kidney tissue and as evidenced by Uemura et al and Pastorek et al the G 250 antigen of Oosterwijk et al [a] identical to the MN protein and is necessarily encoded by the nucleic acid of SEQ ID NO:1. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced anti-idiotypic antibodies of the beta type to an antibody that specifically binds the G 250 protein for active immunotherapy in RCC patients in view of Oosterwijk et al [a] as evidenced by Uemura et al and as evidenced by Pastorek et al in view of Raychaudhuri because Raychaudhuri teach the use of anti-idiotypic antibodies of the

beta type (i.e., internal image) as tumor antigen surrogates, which induce tumor-specific immunity and have a number of advantages including the ability to manufacture anti-idiotypic antibodies on a large scale and the increased immunogenicity of such anti-idiotypic antibodies as compared to natural antigens, which may be difficult to isolate, are not present in significant concentration in tumor masses and are typically poorly immunogenic. Therefore, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success at the time the invention was made to have produced anti-idiotypic antibodies of the beta type to an antibody that specifically binds the G 250 protein produced according to the teachings of Oosterwijk et al [a] for RCC therapy because anti-idiotypic antibodies can be manufactured on a large scale and are more immunogenic compared to natural antigens. Further, one of ordinary skill in the art would have had a reasonable expectation of success in doing so because the teachings of Oosterwijk et al [a] indicate success in producing a monoclonal antibody that specifically binds the G 250 protein using a homogenate of renal cell carcinomas as immunogen and according to Raychaudhuri, "methods for generating such anti-idiotypic antibodies are well known to those of skill in the art" and internal image monoclonal antibodies are being used for active immunotherapy in subjects (column 2, lines 61-65). Thus, it would have been obvious to one skilled in the art at the time the invention was made to have produced anti-idiotypic antibodies of the beta type to an antibody that specifically binds the G 250 protein for active immunotherapy in RCC patients in view of Oosterwijk et al [a] as evidenced by Uemura et al and as evidenced by Pastorek et al and in view of Raychaudhuri.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Applicant's response filed 6/15/05 has been carefully considered, but is deemed not to be persuasive. The response argues the enablement of the G 250 antibody (G 250 hybridoma not deposited until September 2001) (see pages 35-43 of the response filed 6/15/05). In view of the new rejection set forth above these arguments are not relevant to the instant rejection and, it is noted that the features upon which applicant relies (i.e., G 250 monoclonal antibody) is not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The response argues that there is nothing in the art prior to the priority date of the instant application that would suggest to one of ordinary skill in the art how to prepare MN-specific antibodies reproducibly by any procedure and one of skill in the art would not be able to screen for MN-specific antibodies without any knowledge of the MN protein and the Oosterwijk et al [a] reference teaches away from the characteristics of the MN protein. The response points out that inherency may not be established by probabilities or possibilities. The response argues that one of ordinary skill in the art following the teachings of Oosterwijk et al [a] for producing hybridomas and screening antibodies by selecting those that react to renal cell carcinomas but not to normal kidney tissue would produce a very large spectrum of antibody secreting hybridomas

and applicant questions whether or not any of those would be MN specific, stating that "One can only guess." Applicant's arguments suggest that one of ordinary skill in the art at the time the invention was made would not have had a reasonable expectation of success in producing monoclonal antibodies to the MN protein based on the lack of information and specific teachings of the MN protein. In response to applicant's arguments, applicant is reminded that obviousness only requires a reasonable expectation of success, obviousness does not require absolute predictability (MPEP 2143.02). Applicant has not provided any objective evidence that there was no reasonable expectation of success to support a conclusion of nonobviousness. Oosterwijk et al [a] teach an enabling methodology for producing monoclonal antibodies against the G 250 antigen expressed on renal cell carcinomas using a homogenate of primary renal cell carcinomas as immunogen, which does not require prior isolation of the antigen and antibodies produced according to the methodology of Oosterwijk et al [a] bind an antigen uniquely expressed in renal cell carcinomas and one of skill in the art would have had a reasonable expectation of success in producing such antibodies because Oosterwijk et al [a] produced a monoclonal antibody against the G 250 antigen, providing evidence that the methodology would be successful. Further, Applicant is reminded that the claims are drawn to anti-idiotypic antibodies that mimic the MN protein and not antibodies against the MN protein. The teachings of Raychaudhuri regarding the use of anti-idiotypic antibodies of the beta type (i.e., internal image) as tumor antigen surrogates, which induce tumor-specific immunity and have a number of advantages including the ability to manufacture anti-idiotypic antibodies on a

large scale and the increased immunogenicity of such anti-idiotypic antibodies as compared to natural antigens, which may be difficult to isolate, are not present in significant concentration in tumor masses and are typically poorly immunogenic would have motivated one of ordinary skill in the art to produce anti-idiotypic antibodies of the beta type as a surrogate G 250 antigen for active immunotherapy in renal cell carcinoma patients.

Therefore, taken the combined teachings of Oosterwijk et al [a] as evidenced by Uemura et al and as evidenced by Pastorek et al and in view of Raychaudhuri, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and the rejection is maintained.

14. Claims 22, 30, 36-38, 42-43, 46-48 and 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oosterwijk et al [b] (International Journal of Cancer, 38:489-494, 1986, Ids 10/19/2001) as evidenced by Uemura et al (British journal of Cancer, 81(4):741-746, 1999, cited on PTO-892 mailed 3/22/04) and Pastorek et al (Oncogene, 9:2877-2888, 1994, Ids 10/19/2001) and in view of Raychaudhuri et al (US Patent 5,270,202, 3/12/93, cited previously).

The claims and their interpretations have been described supra.

Oosterwijk et al [b] teach a method for producing monoclonal antibodies and antigen-binding fragments thereof against the G 250 antigen present on RCC and absent from normal kidney tissue (see page 489, right column). As evidenced by

Uemura et al the G 250 antigen is identical to MN protein of the present claims (also known as carbonic anhydrase IX; CA IX or CA9) (see page 744, left and right column) and as evidenced by Pastorek et al the MN protein is encoded by SEQ ID NO:1. Thus, as evidenced by Uemura et al and Pastorek et al the G 250 antigen is identical to the MN protein of the present claims and is necessarily encoded by the nucleic acid of SEQ ID NO:1. Oosterwijk et al [b] do not specifically teach an anti-idiotype antibody to an antibody that specifically binds the MN protein. This deficiency is made up for in the teachings of Raychaudhuri.

Raychaudhuri has been described supra.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced anti-idiotypic antibodies of the beta type to an antibody that specifically binds the G 250 protein for active immunotherapy in RCC patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced anti-idiotypic antibodies of the beta type to an antibody that specifically binds the MN protein for active immunotherapy in RCC patients in view of Oosterwijk et al [b] as evidenced by Uemura et al and as evidenced by Pastorek et al in view of Raychaudhuri et al because Oosterwijk et al [b] a process for producing monoclonal antibodies and antigen-binding fragments thereof against the G 250 antigen present on RCCs and absent on normal kidney tissue and as evidenced by Uemura et al and Pastorek et al the G 250 antigen of Oosterwijk et al [b] identical to the MN protein and is necessarily encoded by the nucleic acid of SEQ ID

NO:1. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced anti-idiotypic antibodies of the beta type to an antibody that specifically binds the MN protein for active immunotherapy in RCC patients in view of Oosterwijk et al [b] as evidenced by Uemura et al and as evidenced by Pastorek et al in view of Raychaudhuri because Raychaudhuri teach the use of anti-idiotypic antibodies of the beta type (i.e., internal image) as tumor antigen surrogates, which induce tumor-specific immunity and have a number of advantages including the ability to manufacture anti-idiotypic antibodies on a large scale and the increased immunogenicity of such anti-idiotypic antibodies as compared to natural antigens, which may be difficult to isolate, are not present in significant concentration in tumor masses and are typically poorly immunogenic and Oosterwijk et al [b] teach that the G 250 antigen could not be purified (see page 490, right column). Therefore, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success at the time the invention was made to have produced anti-idiotypic antibodies of the beta type to an antibody that specifically binds the G 250 protein produced according to the teachings of Oosterwijk et al [b] for RCC therapy because anti-idiotypic antibodies can be manufactured on a large scale and the G 250 antigen is difficult to isolate and anti-idiotypic antibodies are more immunogenic compared to natural antigens. Further, one of ordinary skill in the art would have had a reasonable expectation of success in doing so because the teachings of Oosterwijk et al [b] indicate success in producing a monoclonal antibody that specifically binds the G 250 protein using a homogenate of renal cell carcinomas as

immunogen and according to Raychaudhuri, "methods for generating such anti-idiotypic antibodies are well known to those of skill in the art" and internal image monoclonal antibodies are being used for active immunotherapy in subjects (column 2, lines 61-65). Thus, it would have been obvious to one skilled in the art at the time the invention was made to have produced anti-idiotypic antibodies of the beta type to an antibody that specifically binds the MN protein for active immunotherapy in RCC patients in view of Oosterwijk et al [b] as evidenced by Uemura et al and as evidenced by Pastorek et al in view of Raychaudhuri.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

The response filed 6/15/05 has been carefully considered, but is deemed not to be persuasive. The response argues essentially as above as above for Oosterwijk et al [a] and as such, the examiner's rebuttal above applies here as well and the rejection is maintained.

Conclusion

15. Claims 23 and 31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571)

272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to Tony Parks for Art Unit 1643 whose telephone number is 571-272-0543.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER